

U.S. Appl. No. 09/476,485  
Our Ref. No.: PHY-003US1/108236.119  
Amendment and Response dated July 29, 2004  
Reply to Office Action dated April 29, 2004

**Amendments to the Specification:**

Please replace the paragraph at page 32, lines 14-23, with the following amended paragraph:

In accordance with the second aspect of the invention, a nucleic acid encoding a FRIL family member has at least about 50% nucleic acid sequence identity with a nucleic acid encoding another member of the FRIL family, preferably at least about ~~55%~~ 55% nucleic acid sequence identity, more preferably at least about 60% nucleic acid sequence identity, more preferably at least about 65% nucleic acid sequence identity, still more preferably at least about 75% nucleic acid sequence identity, still more preferably at least about 85% nucleic acid sequence identity, and most preferably at least about 95% nucleic acid sequence identity with a nucleic acid encoding another member of the FRIL family. Percentage nucleic acid sequence identity can be determined as described for the first aspect of the invention.

Please replace the paragraph at page 37, lines 8-22, with the following amended paragraph:

In accordance with the third aspect of the invention, by "therapeutically effective amount" is meant a dosage of a composition of a FRIL family member or pharmaceutical formulation comprising a composition of a FRIL family member that is effective to alleviate and/or reduce either a condition whereby the patient's hematopoietic progenitor cells are depleted or a hematopoietic progenitor cell-depleting activity of a therapeutic (*e.g.*, a chemotherapeutic). Preferably, such administration is ~~systematic~~ systemic (*e.g.*, by intravenous injection). When administered systemically, a therapeutically effective amount is an amount of between about 500 ng of the FRIL family member/kg total body weight and about 5 mg/kg total body weight per day. Preferably, a therapeutically effective amount is between about 500 ng/kg and 500 µg/kg total body weight of the FRIL family member per day. Still more preferably, a therapeutically effective amount is between about 5 µg/kg and 50 µg/kg total body weight of the FRIL family member per day. Most preferably, a therapeutically effective amount is an amount that delivers about 50 µg/kg total body weight of the FRIL family member per day.

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Please replace the paragraph bridging pages 39 and 40, with the following amended paragraph:

In some embodiments of the third aspect, the ~~reatment~~ treatment is a radiotherapeutic or a chemotherapeutic treatment, including, without limitation, cytarabine (Ara-C), doxorubicin (Dox), or 5-fluorouracil (5-FU), or a combination of a radiotherapeutic and a chemotherapeutic.

Please replace the paragraph at page 119, lines 14-20, with the following amended paragraph:

Drugs designed to alter signal transduction pathways need to specifically distinguish target cells. FRIL is used as a targeting vehicle to deliver small molecules to Flt3-expressing cells such as stem cells, progenitors, and dendritic cells. FRIL has several advantages for drug delivery: 1) FRIL is specific for Flt3; 2) FRIL is stable in the cytoplasm; 3) FRIL is capable of undergoing conjugation with small molecules; 4) FRIL can be delivered in dose-responsive manner; and 5) FRIL provides specificity for overlapping pathways of signal transduction.